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Development of breast anthropomorphic phantoms for combined PET-Ultrasound elastography imaging

Jun Dang, Philippe Lasaygues, Dachun Zhang, Stefaan Tavernier, Nicoas Felix, Benjamin Frish, Serge Mensah and Mingxi Wan

Abstract—A phantom has been developed for PET/US breast imaging. The phantom reproduces the acoustic and elastic characteristics of human breast tissue, and the different tissues in the phantom can be labeled with ^{18}F FDG. The phantom was imaged with whole body PET/CT and also with Shear Wave Elastography with Supersonic Imagine Aixplorer system. We also test the phantom for other elastography methods such as static elastography. A 6D magnetic positioning system is used for image / volume matching and fusion. This phantom is developed for ClearPEM/US multimodal breast imager.

I. INTRODUCTION

Breast cancer is the 2nd most common type of cancer [1] and the 5th most common cause of cancer death [2]. Breast cancer detection by X-ray mammography and by B-mode ultrasound scanning are in routine clinical use. X-ray mammography has a high sensitivity of about 90% for the detection of breast cancer [3], but its specificity for distinguishing malignant from benign lesions is only about 20~50% (*i.e.*, there are many false positives) [4]. Thus, a large fraction (> 50%) of the suspicious structures identified in mammograms are non-cancerous [5], and further diagnosis is necessary before deciding to treat the patient for cancer. The sensitivity and specificity of PET for detecting breast cancer are reported to be 92%~97% and 78%~90% [6], which is ideal for malignant tumor detection. On the other hand, ultrasound (US) has a diagnostic sensitivity 86%~100% and specificity 80%~100% [7], and has excellent spatial and contrast resolution. It provides anatomical and even functional information (with US contrast agents). In addition US real time imaging is a non-radiating and low-cost technique. This motivates the Crystal Clear Collaboration to undertake the development of a combined breast PET/US scanner (CLEARPEM Sonic System). US elastography imaging, in addition to morphological information provided by US B-mode imaging, provides the tissues' elasticity distribution. Application of this technology to breast imaging has been reported to with promising results [8]. This motivates us to

also consider the combination of PET with US elastography. In this way it will not only be possible to obtain the functional and morphological information, but also the tissue elasticity distribution of the breast.

An anthropomorphic breast gelatin-agar phantom has been developed as part of this project. Acoustical and elasticity characteristics of the phantom will be reported, as well as the results obtained with this phantom on commercial scanners.

II. MATERIALS AND METHOD FOR PHANTOM PREPARATION

We choose (GELITA EUROPE, Ballistic 2, photographic grade) and "high gel Agar"(SIGMA-ALDRICH Co.) to prepare the phantom. We measured the propagation speed of the acoustic waves, the attenuation coefficient and the elasticity (Young's modulus) for several series of samples.

We evaluated samples with gelatin mass percentages from 1% to 15% and with agar mass percentages from 0.5% to 5%. This allowed us to find ingredients ratios that give samples with acoustic and elastic signature close to fat tissue, normal glandular tissue, fibrous/hard tissue and carcinoma in the breast.

The acoustical propagation velocity and the attenuation coefficient of several series of samples were measured using transmission and time of flight techniques using 2 parallel single US transducers immersed in a water tank. We found that the gelatin% fraction in the sample will mainly affects acoustical velocity of the sample and that the agar% fraction has a bigger effect on the attenuation coefficient of the sample.

Gelatin %	Agar %	Mean velocity (m/s)	Real tissue value(m/s)
1~5	0.5~10	1503 \pm 8 ~ 1507 \pm 4	1479 \pm 32 (fat)
10	2~ 7	1526 \pm 7 ~ 1531 \pm 1	1553 \pm 35 (glandular tissue)
15	1.5~7	1540 \pm 4 ~ 1543 \pm 11	1584 \pm 27(fibrous tissue)
18	2~ 7	1550 \pm 7~1559 \pm 9	1550 \pm 35 (carcinoma)
Agar%	Gelatin%	Mean Att(db/MHz/mm)	Real tissue value(db/MHz/mm)
0.5~2	1 ~18	0.05 \pm 0.02~0.08 \pm 0.06	0.05(fat)
5	5~ 16	0.09 \pm 0.01~0.15 \pm 0.01	0.14(tissue)
7	10 ~ 18	0.25 \pm 0.03 ~ 0.30 \pm 0.10	0.3(carcinoma)

TABLE I. PHANTOM ACOUSTIC CHARACTERISTICS

From Table I top 5 rows, we find that as gelatin% increase, the average sound velocity also increases and they can be used to mimic breast fat, glandular tissue, fibrous tissue and

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carcinoma. While for the 6th to 9th rows it shows the average acoustic attenuation coefficient increases with Agar%. The phantom can mimic breast tissues both on velocity and side characteristics.

Once, acoustical characterization was performed the samples elasticity was measured using NEED REFERENCE OF THE TECHNIQUE USED TO MEASURE ELASTICITY). We also tried to find a elasticity correspondence between the phantom and real breast tissue.

(Need a reference of proven elasticity of breast tissues)

Gelatin & agar combination	Acoustical tissue type	Measured Young's modulus(kPa)	Real tissue value (kPa)	Elasticity tissue type
1% gelatin +0.5% agar	Fat tissue	22 ± 2	19±7	Fat tissue
2%gelatin+1%agar	Fat tissue	36 ± 2	—	Fat/glandular tissue
5% gelatin +2% agar	Fat/Glandular tissue	33 ± 1	33±11	Glandular tissue
12% gelatin +4% agar	Glandular tissue	73 ± 9	—	Cancer
15% gelatin +5% agar	Carcinoma	117 ± 8	99±33	Cancer/fibrous tissue

TABLE II. PHANTOM ELASTICITY CHARACTERISTICS

Table II shows the elasticity measurement results of the samples, which could mimic real breast tissues from acoustic point of view. The 2nd column shows what kind of breast tissue they can mimic by acoustical requirements. The last column shows what kind of breast tissue they can mimic by elasticity requirements. The phantom can mimic breast fat medium and carcinoma both by acoustical and elasticity requirements.

Based on these studies we were able to produce a realistic phantom simulating a human breast with a tumor.

The steps in the production of the phantom are listed below:

First, measure 1% gelatin and 0.5% agar and mix them with the correct amount of water, heat the beaker in a microwave oven until the water will just boil. This is for the preparation of the fat medium type background. Put the beaker at room temperature and measure its temperature until it become 40°C. Add F¹⁸FDG into the liquid gel and control the FDG activity 4MBq/ml.

Second, prepare inclusions with tumor type medium. Measure 12% gelatin and 4% agar, and mix them with correct amount of water. Heat them in microwave oven just before it boils. Stir the medium averagely and let it cool down to 45°C. Add F¹⁸FDG in with activity 4 times higher than fat medium, which is 16 MBq/ml. Fill the inclusions into several figure latex hats (don't understand what is a figure latex hat?) and sealed the hats tightly. Put the "inclusion balls" into fridge until they became solid.

Third, remove the inclusion latex skin and emerge them softly into the liquid fat medium when the temperature of fat medium is 40°C.

Fourth, wait for the whole phantom to became totally solid and make a PET scan of it.

Without any care, the phantom will degrade within days after its production. We found that adding Germall-plus [9] as a conservation agent, greatly improved the conservation of the sample. In this way will keep several weeks in a normal fridge.

After the PEM scan, a US scan can be performed immediately or several days later.

III. IMAGING RESULTS

The PET images of the phantoms were obtained with a PHILIPS GEMINI TF 64. For US imaging, as there are several different ways to generate US elastography, we have studied both static elastography by using DP-9900 (Mindray,P.R.China) and Shear Wave Elastography using SuperSonic Imagine Aixplorer system with both 1D and 3D probes (SuperSonic Imagine, Aix en Provence, France) .

A cubic shaped phantom was first prepared to study static elastography and a breast shaped phantom had been prepared later for shear wave elastography.

For static elastography, a linear US probe with center frequency of 7.5 MHz and sampling frequency of 25MHz is used. A rectangular compressor with a polyethylene plate(size 88mm*66mm) is used to enlarge the US probe contact surface between the phantom surface. US probe was fitted inside the compressor by a slot cut. US radio-frequency (RF) data were acquired by a 32 bit data I/O card. Both pre- and post-compression US RF data were acquired. A US probe compression amount of 0.5mm was applied. The strain imaging was based on the RF data from pre-compression and the post-compression. Local tissue displacements were estimated with 1D cross-correlation techniques by comparing the gated pre- and post-compression radiofrequency (RF) signals [10]. For all the elastograms, the length of the correlation window was fixed at 2.5mm, and a overlap window of 80% was used. To remove the signal deformation due to mechanical compression, temporal stretching [11] is conducted on post-compression signals with a stretching factor of the mean strain. After the displacement data were obtained, the axial strain was then computed from the displacement estimates using a third-order optimum low-pass differentiator [12]. The dynamic range (DR) of the static elastogram was set to 0~ 1.5%.

SuperSonic Imagine uses a patented concept to introduce the shear wave into the body : ultrasound beams are successively focalized and sent into different depths of tissue creating a shear wave in the medium. Using ultrafast imaging, the speed of the propagation of the shear wave at every point in the image is measured, and quantitative elasticity map can be deducted in kilo Pascal (kPa).The end result is a real-time, quantifiable, user-independent and reproducible ShearWave™ Elastography information. The technique is totally safe for the patient and respects all acoustic standards defined by the FDA and CE mark. First, we show results from PET and US static elastography. Phantom cross section images from PET and static elastography are listed below. B-mode image tells the anatomical structure, static elastography shows the Strain

(elasticity) distribution, and PET image shows functional information.

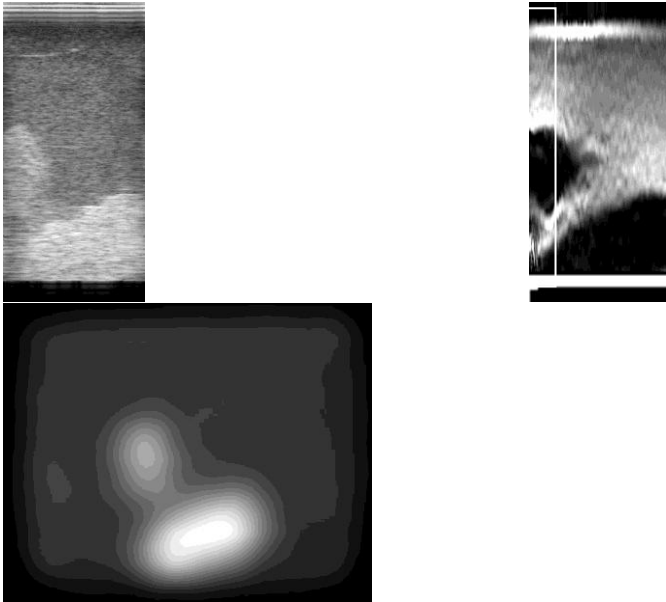


Fig. 1. Cross section phantom images show the US B-mode image, static elastography and whole body PET image. The white box in the whole body image tells the US probe scan region.

Below is displayed the superimposed PET/B-mode/Static Elastography results.

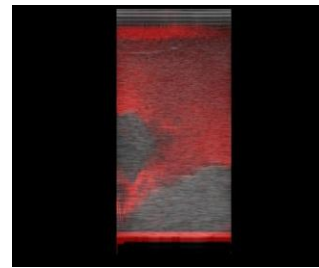
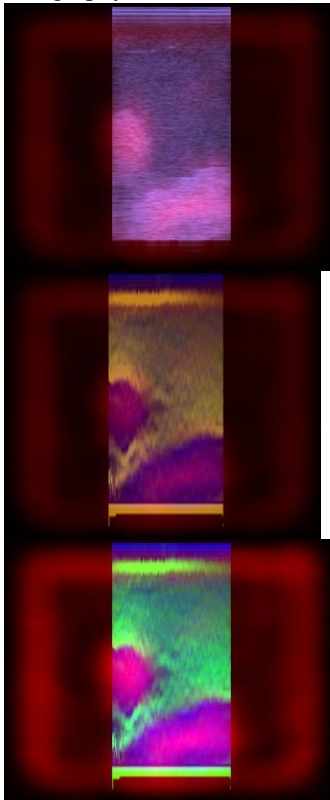


Fig. 2. Comparison of PET/US B-mode/US static elastography results. 1st top left image shows PET/ US B-mode superimposed result. 2nd top right image shows PET/US Static Elastogram superimposed result, 3rd bottom left image shows PET/ US B-mode /US static elastography synthesis superimposed results and the 4th shows US B-mode/US static elastogram superimposed result. In the 4th image, red color stands for strain distribution, it tells the fat tissue mimicking part.

Compared with US B-mode imaging, US elastography shows a better ability to identify tissue differences. For inclusions whose acoustic characteristics is similar with the normal tissue around it (iso-echoic), US B-mode imaging can't show a clear interface between the inclusion and normal background part but static elastography still can distinguish them effectively from their elasticity differences(Fig. 3).

Second we display phantom imaging results from SuperSonic shearwave elastography. As SuperSonic shear wave elastography provides truly quantitative elastography that allows the physician independence from compressional movements inherent in conventional elastography. Fig. 4. shows the image fusion between whole body PET image and shear wave elastography.

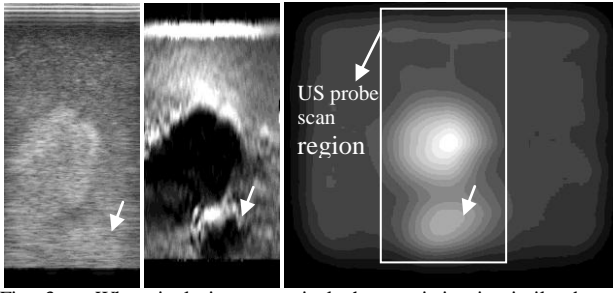


Fig. 3. When inclusion acoustical characteristics is similar between inclusion and background, US B-mode imaging can't distinguish inclusion clearly but static elastography can still show the inclusion from background. White arrows labeled the same inclusion in B-mode image, elastography and PET image.

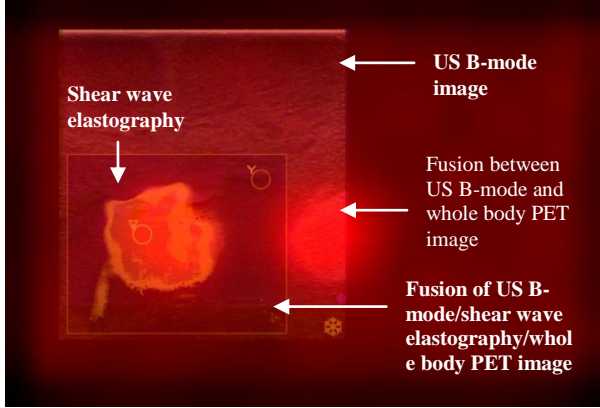


Fig. 4. Image fusion result of US B-mode / shear wave elastography/whole body PET images. This showed triple information of : tissue anatomical information, tissue elasticity information and tissue functional information

IV. IMAGE FUSION BY POSITIONING SYSTEM

As the final purpose for the combination of ClearPEM and SuperSonic shear wave elastography system is to superimpose PET volumes together with US volumes, a 6D magnetic positioning system has been applied to assess the 3D volume registration. The spatial accuracy of the positioning system is 1 mm and 0.1 degree. We first make a breast shaped cone for phantom preparation and added 3 fiducial markers on the cone wall. This is used for registering PET volume. If we scan the phantom by a whole body PET/CT, the fiducial markers can be scanned by the CT scanner, so we can use the image correspondence to choose the needed PET image by CT fiducial marked images. We used the positioning system to record the positions of the fiducial markers together with the 3D US probe, including the special angle of the US probe. With these positions data we can know compared with PET image, where should the US image be superimposed. Note that there is a window on the breast phantom cone for US probe scanning. Although the phantom will have a small deformation by US probe compression, only linear transformation is performed. With SuperSonic system both B-mode volume and elastography volume are simultaneously. Fig. 5. shows the fiducial markers and positioning sensors. And image fusion results are shown in Fig. 6. The result shows an acceptable matching that demonstrates that the 6D positioning system is working properly for PET/US volume matching and registration.



Fig. 5. Fiducial markers and positioning system for image matching

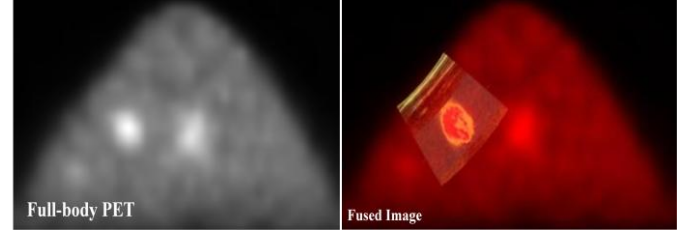


Fig. 6. Whole body PET image and Fused PET/US image. This shows the 6D positioning system works for the image matching case.

V. DISCUSSION AND CONCLUSION

This gelatin-agar PET/US phantom is developed for combination research of a breast PET(ClearPEM) and commercialized US-elastography Aixplorer system (SuperSonic Imagine). The phantom has already been tested by whole body PET and it works well. With the excellent special resolution of ClearPEM($\approx 1.5\text{mm}$), it is ideal to test the performance of ClearPEM with this phantom, e.g. we can prepare tumor type inclusions with different sizes(1mm, 2mm, 3mm, etc.) to mimic the very realistic cases to demonstrate the performances of the ClearPEM system. With this phantom it is also possible to make a benchmarking evaluation between the performance of a commercially available PET/CT and the ClearPEM system. Once volumes are obtained from ClearPEM, the phantom can still be scanned by any US imaging system to get US images for PET/US image fusion study. We already found tumor like inclusion with sizes around 1mm can be detected by SuperSonic shear wave elastography system. The in-vitro performance test of ClearPEM system should be performed in the future with this phantom. The PET/US dual modality system should be integrated together so that simultaneous volumetric imaging could be performed, and the phantom is an ideal training object for volume registration and system performance evaluation.

For the ClearPEM scanning, the patient is laying with a prone position on the bed and the breast will be scanned between two parallel detector heads(Fig. 7). A mechanical arm will be used to hold the US probe between the two detector heads for simultaneous scanning (Fig. 8). A breast shaped cone will be installed on the bed to fit the breast nature shape and different breast sizes (Fig. 9). There will also be a open US scan window on the breast cone wall to fit the US probe (Fig. 10).



Fig. 7

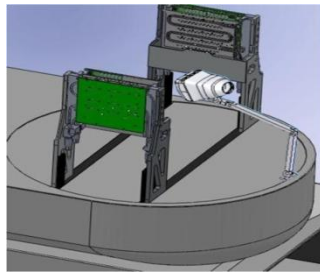


Fig. 8



Fig. 9

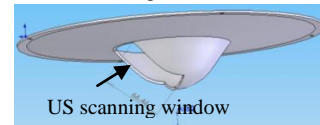


Fig. 10

For conclusion, we have developed a gelatin-agar dual modality phantom for PET/US breast imaging research. This phantom could mimic different breast tissues types such as fat tissue, glandular tissue, fibrous tissue and carcinoma. It works well for whole body PET/CT and for any US imaging system. Phantom should be used to test ClearPEM performance also. A 6D magnetic positioning system has been evaluated for PET/US volume registration and fusion. Further test with ClearPEM system will be performed to optimize accuracy of this positioning system.

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